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=> b reg FILE 'REGISTRY' ENTERED AT 10:54:53 ON 05 DEC 2008 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2008 American Chemical Society (ACS)

(See notes)
hending

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 DEC 2008 HIGHEST RN 1079441-15-8 DICTIONARY FILE UPDATES: 3 DEC 2008 HIGHEST RN 1079441-15-8

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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4.76.600

L6 STR

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GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

82 SEA FILE=REGISTRY SSS FUL L6 STR

L10

G2 11

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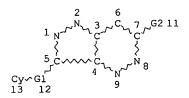
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Dec 2, 2008

10 / 772219

STEREO ATTRIBUTES: NONE L11 STR



See handwritten notes

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STEREO ATTRIBUTES: NONE

41 SEA FILE=REGISTRY SUB=L8 SSS FUL (L10 OR L11)

100.0% PROCESSED 82 ITERATIONS 41 ANSWERS

SEARCH TIME: 00.00.01

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FILE COVERS 1907 - 5 Dec 2008 VOL 149 ISS 24 FILE LAST UPDATED: 4 Dec 2008 (20081204/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitrn fhitstr 116 tot

L16 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:696343 HCAPLUS

DN 141:225525

TI Preparation of pyrazolopyridazines as inhibitors of protein kinases

IN Green, Jeremy; Grey, Ronald; Pierce, Albert C.

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

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                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
           RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
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                                        20040204
      2004WO-US0003061
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os
      MARPAT 141:225525
GΙ
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RN

Ι

AB The title compds. [I; R1 = substituted Ph, alkylphenyl, CH2Ph, etc.; R2 = halo, NO2, CN, etc.; R3 = H, alkyl; X = a bond, O, S, (un)unsubstituted NH; R4 = H, quinazolinyl, pyrimidinyl, etc.] which are inhibitors of protein kinases, particularly inhibitors of GSK mammalian protein kinase, and more particularly inhibitors of GSK-3 mammalian protein kinase, were prepared E.g., a multi-step synthesis of 3-amino-5-(3,4-dimethoxyphenyl)-1,5-dihydropyrazolo[4,3-c]pyridazine-6-one, starting from 3,4-dimethoxyaniline and di-Me acetonediacarboxylate, was given. The representative compds. I were shown to have Ki of < 4.0 μM for GSK-3β. The invention also provides pharmaceutically acceptable compns. comprising the compds. I and methods of utilizing those compds. and compns. in the treatment of various protein kinase mediated disorders.

TT 746647-38-1P 746647-39-2P 746647-40-5P 746647-41-6P 746647-42-7P 746647-43-8P 746647-44-9P 746647-45-0P 746647-46-1P 746647-50-7P 746647-51-8P 746647-52-P 746647-53-0P 746647-51-8P 746647-52-P 746647-62-1P 746647-63-2P 746647-62-1P 746647-63-2P 746647-71-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyridazines as inhibitors of protein kinases) IT ${\bf 338395-98-5}$

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrazolopyridazines as inhibitors of protein kinases) ${\bf 746647-38-1P}$

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolopyridazines as inhibitors of protein kinases) 746647-38-1 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
3-amino-1,5-dihydro-5-(3-methoxyphenyl)- (CA INDEX NAME)

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MeO NH2
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=> b uspatall FILE 'USPATFULL' ENTERED AT 10:56:19 ON 05 DEC 2008 CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATOLD' ENTERED AT 10:56:19 ON 05 DEC 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:56:19 ON 05 DEC 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitrn fhitstr 118 tot

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ANSWER 1 OF 1 USPATFULL on STN 2004:248082 USPATFULL
ΑN
TΙ
       Compositions useful as inhibitors of protein kinases
IN
       Green, Jeremy, Burlington, MA, UNITED STATES
       Grey, Ronald, Cambridge, MA, UNITED STATES
       Pierce, Albert C., Cambridge, MA, UNITED STATES
PΙ
       US-20040192682
                            A1 20040930
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       2004WO-US0003061
                            20040204
       2003US-000445529P
                            20030206 (60)
DT
       Utility
FS
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LREP
       VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
       02139-4242
CLMN
       Number of Claims: 63
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 1928
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides a compound of formula I:
```

or a pharmaceutically acceptable salt or mixtures thereof. These compounds are inhibitors of protein kinases, particularly inhibitors of GSK mammalian protein kinase, and more particularly inhibitors of GSK-3 mammalian protein kinase. The invention also provides pharmaceutically acceptable compositions comprising the compounds of the invention and methods of utilizing those compounds and compositions in the treatment of various protein kinase mediated disorders.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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     6H-Pyrazolo[4,3-c]pyridazin-6-one,
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HCAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr 120 tot

- L20 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
- AN 2002:220584 HCAPLUS
- DN 136:247584
- TI Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
- IN Bebbington, David; Knegtel, Ronald; Golec, Julian M. C.; Li, Pan; Davies, Robert; Charrier, Jean-Damien
- PA Vertex Pharmaceuticals Incorporated, USA
- SO PCT Int. Appl., 356 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 14

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Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substitutedPh, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I (wherein 21 = CR9; Z2 and 23 = N; 24 = CRy]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of $<0.1~\mu\text{M}$ for glycogen synthetase kinase 3β (GSK-3 β) and $0.1-1.0 \mu M$ for Aurora-2. 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo(4,3-c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS 6H-Pyrazolo[4,3-c]pyridazin-6-one, quinazolinyl]amino]- (CA INDEX NAME)

RN 404829-16-9 HCAPLUS

N 404029-10-9 nCAPLOS N 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
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RN 404829-21-6 HCAPLUS

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RN 404829-22-7 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ALL CITATIONS AVAILABLE IN THE RE FORMAT L20 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN 2002:220583 HCAPLUS ΑN 136:247583 ΤI Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease Davies, Robert; Bebbington, David; Knegtel, Ronald; Wannamaker, Marion; IN Li, Pan; Forester, Cornelia; Pierce, Albert; Kay, David Vertex Pharmaceuticals Incorporated, USA PA PCT Int. Appl., 373 pp. SO CODEN: PIXXD2 DΤ Patent LA English FAN.CNT 14 PATENT NO. KIND DATE APPLICATION NO. WO--2002022607 A1 20020321 2001WO-US0028940 20010914 <--ΡI W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

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Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a (un)substituted fused ring containing 0-3 heteroatoms; T=a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring C]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2. 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, (5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-6-0xo-1H-pyrazolo[4,3-c]pyridazin-3-yphenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-y1](2-phenylquinazolin-4-y1)amine 404829-22-7P,
[6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-y1](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS CN 6H-Pyrazolo[4,3~c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

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CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 HCAPLUS

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RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
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     PCT Int. Appl., 355 pp.
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Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4COZ(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N, OR OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 =

independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3= CRx; Z4 = CRy; G = Ring D]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2. 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

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N 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:220581 HCAPLUS

DN 136:247581

TI Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

treatment of cancer, diabetes, and Alzheimer's disease

IN Golec, Julian M. C.; Charrier, Jean-Damien; Knegtel, Ronald; Bebbington,
David; Davies, Robert; Li, Pan

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 14

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phenylquinazolin-4-yl)amine 404829-23-8P,

OS 1

AΒ Title compds. I (wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring $D = \{un\}$ substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SOO-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrazolamines and indazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N; at least one of Z1 or Z3 = N]. Examples include data for approx. 300invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of $< 0.1 \mu M$ for glycogen synthetase kinase 3β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2. 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-y1](2-phenylquinazolin-4-y1)amine. 404829-22-7P,
[6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-y1](2[5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
 (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)
404827-31-2 HCAPLUS
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RN CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 HCAPLUS

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

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404829-22-7 HCAPLUS RN

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:220580 HCAPLUS

DN 136:247606

TI Preparation of 3-(4-pyrimidinylamino)pyrazole derivatives as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treating cancer, diabetes and Alzheimer's disease.

IN Davies, Robert; Bebbington, David; Binch, Haley; Knegtel, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DT Patent

LA English FAN.CNT 14

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The preparation of title compds. I and their pharmaceutically acceptable salts or prodrugs is described [wherein: R1, R2 = dependently form (un)substituted fused, unsatd. or partially unsatd., 5-8 membered carbocyclo ring; R3, R4 = independently H, aliphatic, aryl, heteroaryl, heterocyclyl, or wide variety of functionalized sidechains; or dependently form a fused, 5-8 membered, unsatd. or partially unsatd. ring having 0-3 ring heteroatoms (N, S, O); R5 = fused, (un)substituted 5-7 membered monocyclic ring or 8-10 membered bicyclic ring (aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms (N, S, O))]. For example, chlorination of quinazolone II with phosphorus oxychloride, followed by condensation with 3-amino-5-methylpyrazole afforded claimed compound III. Compds. I are inhibitors of GSK-3 and Aurora-2 protein kinases. The invention also relates to methods of treating diseases associated with these protein kinases, such as diabetes, cancer and Alzheimer's disease. In bioassays, compds. I inhibited the following kinases with Kis reported < 100 nM: GSK-3B (163 compds.), AURORA-2 (65 compds.), CDK-2 (no data), ERK2 (8 compds.), AKT (no data), and Human Src kinase (21 compds.). Claims included 146 specific compds., and 188 examples were given. The syntheses of 6 compds. and 46 intermediates are described.

IT 404827-31-2P 404829-16-9P 404829-17-0P 404829-18-1P 404829-19-2P 404829-21-6P 404829-22-7P 404829-23-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 3-(4-pyrimidinylamino)pyrazole compds. as protein kinase inhibitors)

RN 404827-31-2 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN 404829-16-9 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

404829-19-2 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22~7 HCAPLUS RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN $404829{-}23{-}8$ HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN AN 2002:220579 HCAPLUS

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Title compds: I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)20, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6,

C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un) substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (triazinyl)pyrazolamines and indazolamines I [wherein 21, 22, and 23 = 8, 24 = 8 CRy]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 0.1-1.0 μM for Aurora-2. 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-y1)-[2-(2-trifluoromethylphenyl)quinazolin-4-y1]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-1)phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, $\hbox{\tt [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-pyrazolo[4,3-c]pyridazin-1h-py$ 3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-{(2-phenyl-4-quinazolinyl)amino}- (CA
INDEX NAME)

404829-17-0 HCAPLUS RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-18-1 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

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404829-19-2 HCAPLUS
6H-Pyrazolo[4,3-c]pyridazin-6-one,
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404829-21-6 HCAPLUS

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 HCAPLUS RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 3 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

2002:220578 HCAPLUS AN

DN 136:263164

Preparation of triazolamines as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

Bebbington, David; Knegtel, Ronald; Binch, Haley; Golec, Julian M. C.; Li, TN Pan; Charrier, Jean-Damien

Vertex Pharmaceuticals Incorporated, USA PΑ

PCT Int. Appl., 377 pp. SO

CODEN: PIXXD2

DT Patent LA English FAN.CNT 14

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Triazolamines I and pyrazolamines II (wherein G = Ring C or Ring D; Ring C AB = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6) 2NR6CO, C(R6) 2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (heterocyclyl)triazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; R9 is defined above]. Examples include data for approx. 300 invention compds.

prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK- β 3, Aurora-2, ERK, and Src. For instance, the N-(4-quinazolinyl)-1H-1,2,4-triazol-3-amine III was prepared and exhibited Ki values of < 0.1 μM for glycogen synthetase kinase 3β (GSK-3 β) and 1.0-20 μ M for Aurora-2. **404827-31-2P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (protein kinase inhibitor; preparation of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1, 5- dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

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6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CN 404829-21-6 HCAPLUS
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
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RN 404829-23-8 HCAPLUS

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L20 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

AN 2002:220577 HCAPLUS

DN 136:247579

TI Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

IN Knegtel, Ronald; Bebbington, David; Binch, Hayley; Golec, Julian; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan; Wannamaker, Marion; Forster, Cornelia; Pierce, Albert

PA Vertex Pharmaceuticals Incorporated, USA

SO PCT Int. Appl., 376 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN. CNT 14

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OS MARPAT 136:247579

6H-Pyrazolo[4,3-c]pyridazin-6-one,

AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substitutedPh, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)saturated fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un) substituted fused ring containing 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6) 2NR6SO2NR6, C(R6) 2NR6CONR6, or CONR6; R = H or (un) substitutedaliphatic, (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliphatic), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliphatic group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepared as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrimidinyl- and pyridinyl- pyrazolamines and indazolamines I (wherein Z1 = N, CRa, or CH; Z2 = N or CH; and at least one of Z1 or Z2 = N; Z3 = CRx; Z4 = CRy; Ra = CRyhalo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, etc.; R and R4 are defined above]. Examples include data for approx. 300 invention compds. prepared by a variety of synthetic methods and bioassay results for the inhibition of GSK-β3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepared and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β (GSK-3 β) and 0.1-1.0 μ M for Aurora-2. 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 HCAPLUS

1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 HCAPLUS

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

404829-19-2 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-21-6 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 HCAPLUS RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

INDEX NAME)

404829-23-8 HCAPLUS

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA-INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

1993:482777 HCAPLUS

DN 119:82777

OREF 119:14663a,14666a

ΤI Preparation of photographic cyan couplers

Ikesu, Satoru; Kita, Hiroshi; Kaneko, Yutaka

PΑ

Konica Co., Japan Jpn. Kokai Tokkyo Koho, 13 pp. SO

CODEN: JKXXAF

DΤ Patent

Japanese LA

FAN CNT 1

LIM. CIVI I					
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PI JP0)4307542	Α	19921029	1991JP-000097860	19910404 <
PRAI 1991JP-	-000097860		19910404	< 	
GI					

- Pyrazolopyridazine derivs. (I; R1, R2, Y = H, substituent; X = H, AB substituent leaving upon reaction with the oxidized form of a color developing agent) are prepared I showed excellent stability against heat, humidity, and light. 148665-09-2 148665-15-0 148665-16-1
- IT RL: TEM (Technical or engineered material use); USES (Uses) (photog. cyan coupler) 148665-09-2 HCAPLUS

RN

Benzenesulfonamide, N-[4-[3-[5-(4-bromophenyl)-7-chloro-5,6-dihydro-6-oxo-CN 1H-pyrazolo[4,3-c]pyridazin-3-yl]propyl]phenyl]-4-(dodecyloxy)- (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

 $-(CH_2)_{11}-Me$

RN 148665-15-0 HCAPLUS

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
7-bromo-3-[3-[[2-butoxy-5-(1,1,3,3tetramethylbutyl)phenyl]sulfonyl]propyl]-5-ethenyl-1,5-dihydro- (CA INDEX NAME)

RN 148665-16-1 HCAPLUS

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 7-chloro-3-(dodecylamino)-5-(3-furanyl)-1,5-dihydro- (CA INDEX NAME)

=> b uspatall FILE 'USPATFULL' ENTERED AT 10:57:28 ON 05 DEC 2008 CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATOLD' ENTERED AT 10:57:28 ON 05 DEC 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:57:28 ON 05 DEC 2008 CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr 121 tot

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L21 ANSWER 1 OF 40 USPATFULL on STN AN 2007:309342 USPATFULL
ΤI
            Pyrazole compounds useful as protein kinase inhibitors
            Bebbington, David, Newbury, UNITED KINGDOM
           Binch, Hayley, Harwell, UNITED KINGDOM
           Knegtel, Ronald, Abingdom, UNITED KINGDOM
           Golec, Julian, Ashbury, UNITED KINGDOM
Patel, Sanjay, Abingdom, UNITED KINGDOM
           Charrier, Jean-Damien, Bishop's Itchington, UNITED KINGDOM
            Kay, David, UNITED STATES
            Davies, Robert, Arlington, MA, UNITED STATES
           Li, Pan, Arlington, MA, UNITED STATES
           Wannamaker, Marion, Stow, MA, UNITED STATES
Forster, Cornelia, Pelham, NH, UNITED STATES
            Pierce, Albert, Somerville, MA, UNITED STATES
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A1 20060306 (11)
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           2001US-000286949P
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DT
           Utility
FS
           APPLICATION
           VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
LREP
           02139-4242, US
           Number of Claims: 19
CLMN
ECI.
           Exemplary Claim: 1
DRWN
           No Drawings
LN.CNT 8161
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
           This invention describes novel pyrazole compounds of formula IV:
                              wherein Ring D is a 5-7 membered monocyclic ring or 8-10
           membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or
           carbocyclyl; R.sup.x and R.sup.y are independently selected from
           T-R.sup.3, or taken together with their intervening atoms to form a
            fused, unsaturated or partially unsaturated, 5-8 membered ring having
            1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen; and
           R.sup.2, R.sup.2', T, and R.sup.3 are as described in the specification.
           The compounds are useful as protein kinase inhibitors, especially as
            inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer,
           diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
          c)pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
          404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
          pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
          404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
          c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
          [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
          yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
          [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
          yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
          [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
          c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
          [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
          yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
          [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
          phenylquinazolin-4-yl)amine
              (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes,
              and Alzheimer's disease)
RN
        404827-31-2 USPATFULL
        6H-Pyrazolo[4,3-c]pyridazin-6-one,
CN
            1,5-dihydro-5-phenyl-3-[[2-\{2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(trifluoromethyl)phenyl]-4-[2-(tri
            quinazolinyl]amino]- (CA INDEX NAME)
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RN 404829-16-9 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-17-0 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-{(2-phenyl-4-quinazolinyl)amino}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-.(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
L21 ANSWER 2 OF 40 USPATFULL on STN AN 2006:302298 USPATFULL
         Triazole compounds useful as protein kinase inhibitors
 ΤI
         Bebbington, David, Newbury, UNITED KINGDOM
Knegtel, Ronald, Abingdon, UNITED KINGDOM
 IN
         Binch, Hayley, Harwell, UNITED KINGDOM
         Golec, Julian M. C., Faringdon, UNITED KINGDOM
Li, Pan, Arlington, MA, UNITED STATES
         Charrier, Jean-Damien, Grove, UNITED KINGDOM
                             A1 20061116
A1 20060725 (11)
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         2006US-000492450
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 PRAI
         2000US-000232795P
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         2000US-000257887P
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         2001US-000286949P
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 DT
         Utility
         APPLICATION
  FS
         VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
 LREP
         02139-4242, US
 CLMN
         Number of Claims: 47
         Exemplary Claim: 1
 ECL.
  DRWN
         No Drawings
  LN.CNT 9400
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
         This invention describes novel triazole compounds of formula IX:
 AB
         ##STR1## wherein Z.sup.1 is nitrogen or CR.sup.9 and Z.sup.2 is
         nitrogen or CH, provided that at least one of Z.sup.1 and Z.sup.2 is
         nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl,
         pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring,
         wherein said Ring C has one or two ortho substituents independently
         selected from --\bar{R}.sup.1; Ring D is a 5-7 membered monocyclic ring or
         8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl
         or carbocyclyl; R.sup.x and R.sup.y are independently selected from
         T-R.sup.3, or R.sup.x and R.sup.y are taken together with their
         intervening atoms to form a fused ring; R.sup.1, R.sup.3, and T are as
         described in the specification. The compounds are useful as protein
         kinase inhibitors, especially as inhibitors of GSK-3 and Aurora, for
         treating diseases such as diabetes, cancer, and Alzheimer's disease.
  CAS INDEXING IS AVAILABLE FOR THIS PATENT.
  IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
        c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
        404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
        pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
        404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
        c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1p,
        [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
        yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
        [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
        yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-17-0 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-18-1 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

6H-Pyrazolo(4,3-c]pyridazin-6-one, 1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino]- (CA

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

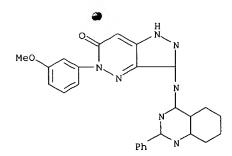
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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L21
     ANSWER 3 OF 40 USPATFULL on STN
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ΤI
       Pyrazole compounds useful as protein kinase inhibitors
IN
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FS
       APPLICATION
       Andrew S. Marks, Esq., VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly
LREP
       Street, Cambridge, MA, 02139-4242
CLMN
       Number of Claims: 36
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula III:
AB
       ##STR1##
```

wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered carbocyclo ring; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-16-9 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-17-0 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

404829-18-1 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino)- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-23-8 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 4 OF 40 USPATFULL on STN 2004:286776 USPATFULL ΤI Pyrazole compounds useful as protein kinase inhibitors Bebbington, David, Newbury Berkshire, UNITED KINGDOM TN Binch, Hayley, Harwell, UNITED KINGDOM Knegtel, Ronald, Abingdom, UNITED KINGDOM Golec, Julian, Swinden Wilts, UNITED KINGDOM Patel, Sanjay, Abingdom, UNITED KINGDOM Charrier, Jean-Damien, Southam, UNITED KINGDOM Kay, David, Church Path, UNITED KINGDOM Davies, Robert, Arlington, MA, UNITED STATES Li, Pan, Arlington, MA, UNITED STATES Wannamaker, Marion, Stow, MA, UNITED STATES Forster, Cornelia, Pelham, NH, UNITED STATES Pierce, Albert, Somerville, MA, UNITED STATES ΡI US-20040224944 A1 20041111 B2 20060307 A1 20030722 (10) US----7008948 2003US-000624800 AΤ Division of Ser. No. 2001US-000952671, filed on 14 Sep 2001, GRANTED, RLI Pat. No. US----6660731 2000US-000232795P 20000915 (60) PRAI 2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60) DT Utility APPLICATION FS VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA, LREP 02139-4242 Number of Claims: 28 CLMN Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 8533

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula IV: ##STR1##

wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T-R.sup.3, or taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered ring having 1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen; and R.sup.2, R.sup.2', T, and R.sup.3 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c}pyridazin-3-y1)-{2-(2-trifluoromethylphenyl)quinazolin-4-y1}amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl) amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC, DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

404829-17-0 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-18-1 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

RN 404829-21-6 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 5 OF 40 USPATFULL on STN

2004:274312 USPATFULL AN

Pyrazole compounds useful as protein kinase inhibitors TT

Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM

Golec, Julian, Swindon, UNITED KINGDOM Miller, Andrew, Didcot, UNITED KINGDOM

Knegtel, Ronald, Abingdon, UNITED KINGDOM

US-20040214814 ΡI

A1 20041028 A1 20011219 (10) 2001US-000026992 ΑI

PRAI 2000US-000257887P 20001221 (60)

2001US-000286949P 20010427 (60) DT Utility APPLICATION FS LREP Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge, MA, 02139-4242 CLMN Number of Claims: 27 ECL Exemplary Claim: 1 DRWN No Drawings LN.CNT 8610 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention describes novel pyrazole compounds of formula IIIc: wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x, R.sup.y, R.sup.2, and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-lHpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine $(protein\ kinase\ inhibitor;\ preparation\ of\ heterocyclylpyrazolamines\ and$ analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPATFULL RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-17-0 USPATFULL

CN . 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-21-6 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

ANSWER 6 OF 40 USPATFULL on STN L21

2004:216032 USPATFULL AN

Pyrazole compounds useful as protein kinase inhibitors ΤI

Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM Golec, Julian, Swindon, UNITED KINGDOM Pierard, Francoise, Drayton, UNITED KINGDOM

US-20040167141 A1 20040826 PΙ US----7427681

B2 20080923 A1 20040210 (10) 2004US-000775699 ΑI

Division of Ser. No. 2001US-000034019, filed on 20 Dec 2001, GRANTED, RLI

```
Pat. No. US----6727251
PRAI
       2000US-000257887P
                           20001221 (60)
                           20010427 (60)
       2001US-000286949P
DT
       Utility
FS
       APPLICATION
       VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
LREP
       02139-4242
CLMN
       Number of Claims: 31
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 2292
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ΑB
       This invention describes novel pyrazole compounds of formula II:
       wherein Z.sup.1 is nitrogen or CR.sup.8; Q is --S--, --O--,
       --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D
       is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring
       selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.y, R.sup.2, and R.sup.2' are as described in the specification.
       The compounds are useful as protein kinase inhibitors, especially as
       inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer,
       diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl] (2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl] (2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPATFULL
RN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
CN
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-.
       quinazolinyl]amino]- (CA INDEX NAME)
```

RN 404829-17-0 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

404829-21-6 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

ANSWER 7 OF 40 USPATFULL on STN L21

2004:204001 USPATFULL ΑN

TI Pyrazole compounds useful as protein kinase inhibitors

Bebbington, David, Newbury, UNITED KINGDOM IN

Charrier, Jean-Damien, Wantage, UNITED KINGDOM

ΡI US-20040157893

A1 20040812 A1 20031125 (10) 2003US-000722374 ΑT

Continuation of Ser. No. 2001US-000034683, filed on 20 Dec 2001, RLI

GRANTED, Pat. No. US----6656939

2000US-000257887P 20001221 (60) PRAI 2001US-000286949P

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05/12/2008 Page 71

20010427 (60)

```
DT
       Utility
       APPLICATION
FS
       VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
LREP
       02139-4242
CLMN
       Number of Claims: 26
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 2148
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula III:
       ##STR1##
       wherein Z.sup.1, Z.sup.2 and Z.sup.3 are as described in the
       specification; Q is -S-, -O-, -N(R.sup.4)-, or -CH(R.sup.6)-; R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or
       8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl
       or carbocyclyl; and R.sup.2 and R.sup.2' are as described in the
       specification. The compounds are useful as protein kinase inhibitors,
       especially as inhibitors of Aurora-2 and GSK-3, for treating diseases
       such as cancer, diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      (5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPATFULL
CN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-{[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

404829-17-0 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino}-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-21-6 .USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3- . (trifluoromethyl)phenyl]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 8 OF 40 USPATFULL on STN 2004:172617 USPATFULL AN Pyrazole compounds useful as protein kinase inhibitors TI Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM A1 20040708 B2 20060808 US-20040132781 PΙ US----7087603 2003US-000736426 A1 20031215 (10) ΑI Continuation of Ser. No. 2001US-000026966, filed on 19 Dec 2001, RLI ABANDONED <--2000US-000257887P 20001221 (60) PRAI

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10 / 772219
       2001US-000286949P
                            20010427 (60)
DT
       Utility
       APPLICATION
FS
LREP
       VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
       02139-4242
CLMN
       Number of Claims: 29
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8905
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AR
       This invention describes novel pyrazole compounds of formula IV:
       wherein Z.sup.1 or Z.sup.2 is nitrogen, Q is --S--, --O--,
       --N(R.sup.4)--, --C(R.sup.6').sub.2--, 1,2-cyclopropanediyl,
       1,2-cyclobutanediyl, or 1,3-cyclobutanediyl, and R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered
       bicyclic ring selected from aryl, heteroaryl, heterocyclyl or
       carbocyclyl; R.sup.x and R.sup.y are independently selected from
       T-R.sup.3 or L-Z-R.sup.3, or R.sup.x and R.sup.y are taken together with
       their intervening atoms to form a fused, unsaturated or partially
       unsaturated, 5-7-membered ring having 0-3 heteroatoms; and R.sup.2 and
       R.sup.2' are as described in the specification. The compounds are useful
       as protein kinase inhibitors, especially as inhibitors of Aurora-2 and
       GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's
       disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
```

yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,

yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,

quinazolinyl]amino]- (CA INDEX NAME)

phenylquinazolin-4-yl)amine

RN CN ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

[5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-

[5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-

[6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-

[6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,

404829-17-0 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-21-6 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 9 OF 40 USPATFULL on STN

2004:152232 USPATFULL AN

Pyrazole compounds useful as protein kinase inhibitors ΤI

IN Davies, Robert, Arlington, MA, UNITED STATES Bebbington, David, Berkshire, UNITED KINGDOM Knegtel, Ronald, Abingdom, UNITED KINGDOM Wannamaker, Marion, Stow, MA, UNITED STATES Li, Pan, Arlington, MA, UNITED STATES Forster, Cornelia, Pelham, NH, UNITED STATES Pierce, Albert, Somerville, MA, UNITED STATES

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B2 20080624
A1 20031023 (10)
       US----7390815
ΑI
       2003US-000692355
       Division of Ser. No. 2001US-000955601, filed on 14 Sep 2001, GRANTED,
RLT
       Pat. No. US----6696452
PRAI .
       2000US-000232795P
                            20000915 (60)
       2000US-000257887P
                            20001221 (60)
       2001US-000286949P
                            20010427 (60)
DT
       Utility
       APPLICATION
FS
       VERTEX PHARMACEUTICALS INC., 130 WAVERLY STREET, CAMBRIDGE, MA,
LREP
       02139-4242
CLMN
       Number of Claims: '34
ECL:
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula II:
```

wherein Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, and R.sup.2, R.sup.2', R.sup.x, and R.sup.y are as described in the specification. Ring C has an ortho substituent and is optionally substituted in the non-ortho positions. R.sup.2 and R.sup.2' are optionally taken together with their intervening atoms to form a fused ring system, such as an indazole ring; and R.sup.x and R.sup.y are optionally taken together with their intervening atoms to form a fused ring system, such as a quinazoline ring. The compounds are useful as protein kinase inhibitors, especially as inhibitors of GSK-3, for treating diseases such as diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo(4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo(4,3-c)pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo(4,3-c)pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN $4\,04\,82\,9-16-9$ USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA
 INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

RN 404829-21-6 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-

(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
L21 ANSWER 10 OF 40 USPATFULL on STN
       2004:127517 USPATFULL
ΑN
TΙ
       Triazole compounds useful as protein kinase inhibitors
IN
       Bebbington, David, Newbury Berkshire, UNITED KINGDOM
       Knegtel, Ronald, Abingdom, UNITED KINGDOM
       Binch, Hayley, Harwell Oxon, UNITED KINGDOM
       Golec, Julian, Asbury Swinden, UNITED KINGDOM
       Li, Pan, Arlington, MA, UNITED STATES
       Charier, Jean-Damien, Bishop's Itchington, UNITED KINGDOM
       US-20040097501
                           A1 20040520
PΙ
       US----7115739
                           B2 · 20061003
                           A1 20010914 (9)
       2001US-000953471
AΙ
       2000US-000232795P
                           20000915 (60)
PRAT
       2000US-000257887P
                           20001221 (60)
       2001US-000286949P
                           20010427 (60)
       Utility
DТ
       APPLICATION
FS
T.RE.P
       VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA,
       02130-4646
CLMN
       Number of Claims: 47
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 9118
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel triazole compounds of formula IX:
       ##STR1##
       wherein Z.sup.1 is nitrogen or CR.sup.9 and Z.sup.2 is nitrogen or CH,
       provided that at least one of Z.sup.1 and Z.sup.2 is nitrogen; G is Ring
       C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl,
       pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has
       one or two ortho substituents independently selected from --R.sup.1;
       Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring
       selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and
       R.sup.y are independently selected from T-R.sup.3, or R.sup.x and
       R.sup.y are taken together with their intervening atoms to form a fused
       ring; R.sup.1, R.sup.3, and T are as described in the specification. The
       compounds are useful as protein kinase inhibitors, especially as
       inhibitors of GSK-3 and Aurora, for treating diseases such as diabetes,
       cancer, and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c|pyridazin-3-yl)-(2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
         (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPATFULL
RN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
CN
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

404829-16-9 USPATFULL RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-17-0 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

404829-19-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)
```

```
L21 ANSWER 11 OF 40 USPATFULL on STN
       2003:153422 USPATFULL
ΑN
TΙ
       Pyrazole compounds useful as protein kinase inhibitors
ΤN
       Bebbington, David, Newbury, UNITED KINGDOM
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
                           A1 20030605
РΤ
       US-20030105090
       2001US-000026966
                           A1 20011219 (10)
ΑТ
PRAI
       2000US-000257887P
                           20001221 (60)
       2001US-000286949P
                           20010427 (60).
DT
       Utility
       APPLICATION
FS
LREP
       Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge,
       MA, 02139-4242
CLMN
       Number of Claims: 29
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 9063
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       This invention describes novel pyrazole compounds of formula IV:
```

wherein Z.sup.1 or Z.sup.2 is nitrogen, Q is --S--, --O--, --N(R.sup.4)--, --C(R.sup.6).sub.2--, 1,2-cyclopropanediyl, 1,2-cyclobutanediyl, or 1,3-cyclobutanediyl, and R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T-R.sup.3 or L-Z-R.sup.3, or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

```
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
```

RN 404829-19-2 USPATFULL

N 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 12 OF 40 USPATFULL on STN

AN 2003:120843 USPATFULL

Pyrazole compounds useful as protein kinase inhibitors

IN Davies, Robert, Arlington, MA, UNITED STATES

Li, Pan, Arlington, MA, UNITED STATES

PI US-20030083327 A1 20030501

US----6610677 B2 20030826

AI 2001US-000952833 A1 20010914 (9) <-PRAI 2000US-000232795P 20000915 (60) <--

PRAI 2000US-000232795P 20000915 (60) <-2000US-000257887P 20001221 (60) <-2001US-000286949P 20010427 (60) <--

DT Utility

TТ

FS APPLICATION

LREP VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA,

02130-4646 CLMN Number of Claims: 25

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 8910

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compositions comprising a pharmaceutically acceptable carrier and a compound of formula VIII: ##STR1##

wherein Z.sup.1 is N or C--R.sup.9, Z.sup.2 is N or CH, and Z.sup.3 is N or C--R.sup.x, provided that one of Z.sup.1 and Z.sup.3 is nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.x, R.sup.1, R.sup.2, R.sup.2', R.sup.3, and R.sup.9 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-lHpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
[5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
[5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
[6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
[6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3-

yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
[5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (CA INDEX NAME)

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-23-8 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 13 OF 40 USPATFULL on STN

AN 2003:113534 USPATFULL

TI Pyrazole compounds useful as protein kinase inhibitors

IN Bebbington, David, Newbury, UNITED KINGDOM
Charrier, Jean-Damien, Wantage, UNITED KINGDOM
Davies, Robert, Arlington, MA, UNITED STATES
Golec, Julian M.C., Swindon, UNITED KINGDOM
Kay, David, Purton, UNITED KINGDOM

Knegtel, Ronald, Abingdon, UNITED KINGDOM

Patel, Sanjay, Abingdon, UNITED KINGDOM

PI US-20030078275 A1 20030424

US----6653301 B2 20031125

AI 2001US-000027001 A1 20011219 (10) <-PRAI 2000US-000257887P 20001221 (60) <--

2001US-000286949P 20010427 (60) <-

DT Utility

FS APPLICATION

LREP Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge, MA, 02139-4242

CLMN Number of Claims: 30

ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 9081

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula IIa: ##STR1##

wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

[5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino](CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-21-6 USPATFULL.
6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-23-8 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 14 OF 40 USPATFULL on STN

2003:113425 USPATFULL AΝ

TΤ Pyrazole compounds useful as protein kinase inhibitors

Davies, Robert, Arlington, MA, UNITED STATES IN Bebbington, David, Newbury, UNITED KINGDOM Knegtel, Ronald, Abingdom, UNITED KINGDOM Wannamaker, Marion, Stow, MA, UNITED STATES Li, Pan, Arlington, MA, UNITED STATES Forster, Cornelia, Pelham, NH, UNITED STATES

Pierce, Albert, Somerville, MA, UNITED STATES

ΡI US-20030078166 A1 20030424 US----6696452 B2 20040224

20010914 (9) 2001US-000955601 AΤ A1

2000US-000232795P PRAI 20000915 (60) 2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60)

DТ Utility

APPLICATION FS

LREP VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA, 02130-4646

CT.MN Number of Claims: 34

ECL Exemplary Claim: 1

No Drawings

LN.CNT 8804

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention describes novel pyrazole compounds of formula II:

wherein Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, and R.sup.2, R.sup.2', R.sup.x, and R.sup.y are as described in the specification. Ring C has an ortho substituent and is optionally substituted in the non-ortho positions. R.sup.2 and R.sup.2' are optionally taken together with their intervening atoms to form a fused ring system, such as an indazole ring; and R.sup.x and R.sup.y are optionally taken together with their intervening atoms to form a fused ring system, such as a quinazoline ring. The compounds are useful as protein kinase inhibitors, especially as inhibitors of GSK-3, for treating diseases such as diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)~[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,

[6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
[6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
[5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
(protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404827-31-2 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[[2-(2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-17-0 USPATFULL CN 6H-Pyrazolo(4,3-c)pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-18-1 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

```
ANSWER 15 OF 40 USPATFULL on STN
L21
       2003:106775 USPATFULL
ΤI
       Pyrazole compounds useful as protein kinase inhibitors
       Bebbington, David, Newbury Berkshire, UNITED KINGDOM
TN
       Binch, Hayley, Harwell Oxon, UNITED KINGDOM
       Knegtel, Ronald, Abingdom, UNITED KINGDOM
       Golec, Julian, Ashbury, UNITED KINGDOM
       Patel, Sanjay, Abingdom, UNITED KINGDOM
       Charrier, Jean-Damien, Bishop's Itchington, UNITED KINGDOM
       Kay, David, Church Path, UNITED KINGDOM
       Davies, Robert, Arlington, MA, UNITED STATES
       Li, Pan, Arlington, MA, UNITED STATES
       Wannamaker, Marion, Stow, MA, UNITED STATES
       Forster, Cornelia, Pelham, NH, UNITED STATES
       Pierce, Albert, Somerville, MA, UNITED STATES
                           A1 20030417
B2 20031209
PI
       US-20030073687
       US----6660731
ΑI
       2001US-000952671
                           Αl
                              20010914 (9)
                           20000915 (60)
       2000US-000232795P
PRAI
       2000US-000257887P
                           20001221 (60)
       2001US-000286949P
                           20010427 (60)
DT
       Utility
FS
       APPLICATION
LREP
       VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA,
       02130-4646
CLMN
       Number of Claims: 25
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula IV:
       ##STR1##
```

wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T-R.sup.3, or taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered ring having

1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen; and R.sup.2, R.sup.2, T, and R.sup.3 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPATFULL RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-17-0 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino](CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-22-7 USPATFULL RN

6H-Pyrazolo(4,3-c)pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 16 OF 40 USPATFULL on STN

2003:93621 USPATFULL AN

Pyrazole compounds useful as protein kinase inhibitors ΤI

IN Davies, Robert, Arlington, MA, UNITED STATES

Li, Pan, Arlington, MA, UNITED STATES

Al 20030403 US-20030064982 PT

Al 20010914 (9) 2001US-000952875 ΑI

2000US-000232795P 20000915 (60) PRAI 2000US-000257887P 20001221 (60)

2001US-000286949P 20010427 (60)

DTUtility

APPLICATION FS

VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA, LREP 02130-4646

CLMN Number of Claims: 25

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 8570

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention describes novel protein kinase inhibitors of formula VII: AB ##STR1##

wherein G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.y is T-R.sup.3"; T is a valence bond or a C.sub.1-4 alkylidene chain; R.sup.3" is an optionally substituted group selected from C.sub.1-6 aliphatic, C.sub.3-10 carbocyclyl, C.sub.6-10 aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms; and R.sup.1, R.sup.2, and R.sup.2' are as

described in the specification. The protein kinase are useful for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo(4,3-c)pyridazin-3yl)(2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-lH-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl) amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPATFULL RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-17-0 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-18-1 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-{(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-22-7 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-{(2-phenyl-4-quinazolinyl)amino}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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L21 ANSWER 17 OF 40 USPATFULL on STN
       2003:93620 USPATFULL
AN
ΤI
       Pyrazole compounds useful as protein kinase inhibitors
       Knegtel, Ronald, Abingdom, UNITED KINGDOM
Bebbington, David, Newbury Berkshire, UNITED KINGDOM
IN
       Binch, Hayley, Oxon, UNITED KINGDOM
       Golec, Julian, Swinden, UNITED KINGDOM
       Patel, Sanjay, Oxon, UNITED KINGDOM
       Charrier, Jean-Damien, Bishop's Itchington, UNITED KINGDOM
       Kay, David, Purton Wiltshire, UNITED KINGDOM
       Davies, Robert, Arlington, MA, UNITED STATES
       Li, Pan, Arlington, MA, UNITED STATES
Wannamaker, Marion, Stow, MA, UNITED STATES
       Forster, Cornelia, Pelham, NH, UNITED STATES
       Pierce, Albert, Somerville, MA, UNITED STATES
       US-20030064981
PΤ
                            A1 20030403
       US----6613776
                             B2 20030902
       2001US-000952836
                                 20010914 (9)
ΑI
                             A1
       2000US-000232795P
                             20000915 (60)
PRAI
       2000US-000257887P
                             20001221 (60)
       2001US-000286949P
                             20010427 (60)
DT
       Utility
       APPLICATION
FS
LREP
       VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA,
       02130-4646
CLMN
       Number of Claims: 31
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8962
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention describes novel pyrazole compositions comprising a
```

pharmaceutically acceptable carrier and a compound of formula V: ##STR1##

wherein Z.sup.1 is N, CR.sup.a, or CH, and Z.sup.2 is N or CH, provided one of Z.sup.1 and Z.sup.2 is nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T--R.sup.3, or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused ring; and R.sup.1, R.sup.2, R.sup.2', R.sup.3, and T are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN CN ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-17-0 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-18-1 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-

(CA INDEX NAME)

RN 404829-21-6 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NÂME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

ANSWER 18 OF 40 USPATFULL on STN L21

2003:79141 USPATFULL ΑN

ΤI

Pyrazole compounds useful as protein kinase inhibitors Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM Davies, Robert, Arlington, MA, UNITED STATES Everitt, Simon, Beaconsfield, UNITED KINGDOM Kay, David, Purton, UNITED KINGDOM

Knegtel, Ronald, Abingdon, UNITED KINGDOM Patel, Sanjay, Abingdon, UNITED KINGDOM US-20030055068 Al 20030320

PΙ

US----6989385 B2 20060124 2001US-000026967 A1 20011219 (10) AΤ 2000US-000257887P PRAI 20001221 (60) <--2001US-000286949P 20010427 (60) DT Utility FS APPLICATION LREP Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge, MA, 02139-4242 CLMN Number of Claims: 39 ECL Exemplary Claim: 1 DRWN No Drawings LN.CNT 8979 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention describes novel pyrazole compounds of formula IIc: ##STR1##

wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-y1)-[2-(2-trifluoromethylphenyl)quinazolin-4-y1]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

404829-17-0 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-18-1 USPATFULL RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-21-6 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino)- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 19 OF 40 USPATFULL on STN AN 2003:79117 USPATFULL Pyrazole compounds useful as protein kinase inhibitors TI Davies, Robert, Arlington, MA, UNITED STATES Li, Pan, Arlington, MA, UNITED STATES IN Golec, Julian, Ashbury, UNITED KINGDOM US-20030055044 ΡI A1 20030320 US----6638926 B2 20031028 ΑI 2001US-000953505 Al 20010914 (9) 2000US-000232795P PRAI 20000915 (60) 2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60)

DТ Utility FS APPLICATION VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA, LREP 02130-4646 CLMN Number of Claims: 58 Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 9881 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention provides novel pyrazole compounds that are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3. The compounds may be used to treat abnormal physiological function leading to diseases such as cancer, diabetes and Alzheimer's disease. The compounds are represented by formula VI: wherein G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from $--\bar{R}$.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.y is T--R.sup.3'; T is a valence bond or a C.sub.1-4 alkylidene chain; R.sup.3 is an optionally substituted group selected from C.sub.1-6 aliphatic, C.sub.3-10 carbocyclyl, C.sub.6-10 aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms; and R.sup.1, R.sup.2, and R.sup.' are as described in the specification. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN

404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

404829-17-0 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-18-1 USPATFULL

RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA)INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

404829-21-6 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 20 OF 40 USPATFULL on STN

2003:51585 USPATFULL ΑN

Pyrazole compounds useful as protein kinase inhibitors TΙ

Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM Golec, Julian, Swindon, UNITED KINGDOM Miller, Andrew, Didcot, UNITED KINGDOM

Knegtel, Ronald, Abingdon, UNITED KINGDOM

US-20030036543 ΡI

A1 20030220 B2 20031216

US----6664247

2001US-000025164 ΑI

A1 20011219 (10)

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20001221 (60)
PRAI
       2000US-000257887P
       2001US-000286949P
                           20010427 (60)
DΤ
       Utility
       APPLICATION
FS
LREP
       Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge,
       MA, 02139-4242
CLMN
       Number of Claims: 28
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8794
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula IIIa:
       ##STR1##
```

Wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.X, R.sup.y, R.sup.2, and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

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CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
RN
     404827-31-2 USPATFULL
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino] - (CA INDEX NAME)
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-17-0 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

RN404829-21-6 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-(3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 21 OF 40 USPATFULL on STN

2003:30936 USPATFULL ΑN

Pyrazole compounds useful as protein kinase inhibitors TΙ

IN Bebbington, David, Newbury, UNITED KINGDOM Charrier, Jean-Damien, Wantage, UNITED KINGDOM

Golec, Julian, Swindon, UNITED KINGDOM

Pierard, Francoise, Drayton, UNITED KINGDOM ΡI

US-20030022885 A1 20030130 US----6727251

B2 20040427 A1 20011220 (10) ΑI 2001US-000034019 2000US-000257887P 20001221 (60)

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2001US-000286949P 20010427 (60)
DT
       Utility
       APPLICATION
FS
       Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge,
LREP
       MA, 02139-4242
CLMN
       Number of Claims: 31
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 2271
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula II:
       wherein Z.sup.1 is nitrogen or CR.sup.8; Q is --S--, --O--,
       --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D
       is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring
       selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.y, R.sup.2, and R.sup.2' are as described in the specification.
       The compounds are useful as protein kinase inhibitors, especially as
       inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer,
       diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPATFULL
RN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPATFULL RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-17-0 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-{(2-phenyl-4-quinazolinyl)amino}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-{(2-phenyl-4-quinazolinyl)amino}-(CA INDEX NAME)

RN 404829-21-6 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPATFULL

CN 6H-Pyrazolo(4,3-c)pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 22 OF 40 USPATFULL on STN 2003:4125 USPATFULL AN Pyrazole compounds useful as protein kinase inhibitors TI ΙN Bebbington, David, Newbury, UNITED KINGDOM Charrier, Jean-Damien, Wantage, UNITED KINGDOM US-20030004164 Al 20030102 A1 20030102 B2 20031202 PΙ US----6656939 2001US-000034683 A1 20011220 (10) ΑI PRAI 2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60) DΤ Utility

FS APPLICATION LREP Tina Powers, VERTEX PHARMACEUTICALS INC., 130 Waverly Street, Cambridge, MA, 02139-4242 CLMN Number of Claims: 26 Exemplary Claim: 1 ECL DRWN No Drawings LN.CNT 2215 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention describes novel pyrazole compounds of formula III: wherein Z.sup.1, Z.sup.2, and Z.sup.3 are as described in the specification; Q is --S--, --O--, --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease. CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPATFULL 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-

quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-16-9 USPATFULL
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-17-0 USPATFULL

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-18-1 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-21-6 USPATFULL RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPATFULL RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPATFULL RN CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 23 OF 40 USPATFULL on STN AN 2003:4122 USPATFULL

ΤI Pyrazole compounds useful as protein kinase inhititors

Bebbington, David, Newbury, UNITED KINGDOM IN Charrier, Jean-Damien, Wantage, UNITED KINGDOM Golec, Julian, Swindon, UNITED KINGDOM Green, Jeremy, Burlington, MA, UNITED STATES Kay, David, Wiltshire, UNITED KINGDOM Knegtel, Ronald, Abingdon, UNITED KINGDOM Miller, Andrew, Upton Didcot, UNITED KINGDOM Tomlison, Ronald, Marlborough, MA, UNITED STATES

Li, Pan, Arlington, MA, UNITED STATES PΤ US-20030004161 20030102 <--A1 US----6653300 B2 20031125 20011219 (10) ΑT 2001US-000026975 A1 <--2000US-000257887P 20001221 (60) PRAI 2001US-000286949P 20010427 (60) DΨ Utility APPLICATION FS VERTEX PHARMACEUTICALS INCORPORATED, 130 Waverly Street, Cambridge, MA, LRĖP 02130-4646 CLMN Number of Claims: 43 ECL Exemplary Claim: 1 DRWN No Drawings LN.CNT 9244 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention describes novel pyrazole compounds of formula I': ##STR1##

wherein Q' is --O-, --C(R.sup.6').sub.2--, 1,2-cyclopropanediyl, 1,2-cyclobutanediyl, or 1,3-cyclopropanediyl, and R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T-R.sup.3 or L-Z-R.sup.3 or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPATFULL CN 6H-Pyrazolo(4,3-c)pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-

quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN $4\,04\,82\,9-16-9$ USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPATFULL

RN 404829-17-0 USPATFULL CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPATFULL

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

RN 404829-21-6 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPATFULL

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPATFULL RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
L21
    ANSWER 24 OF 40 USPAT2 on STN
       2005:5004 USPAT2
AN
TI
       Pyrazolylamine substituted quinazoline compounds useful as protein
       kinase inhibitors
       Bebbington, David, Newbury, UNITED KINGDOM
IN
       Binch, Hayley, Harwell, UNITED KINGDOM
       Knegtel, Ronald, Abingdon, UNITED KINGDOM
       Golec, Julian M. C., Swinden, UNITED KINGDOM
       Patel, Sanjay, Abingdon, UNITED KINGDOM
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
       Kay, David, Purton, UNITED KINGDOM
       Davies, Robert J., Arlington, MA, UNITED STATES
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S.
PΑ
       corporation)
ΡI
       US----7098330
                           B2 20060829
       2001US-000952878
AΙ
                               20010914 (9)
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PRAI
       2001US-000286949P
                           20010427 (60)
                                                                     <--
       2000US~000257887P
                           20001221 (60)
       2000US-000232795P
                           20000915 (60)
DT
       Utility
FS
       GRANTED
       Primary Examiner: McKenzie, Thomas C.
EXNAM
LREP
       Vertex Pharmaceuticals Incorporated
       Number of Claims: 15
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 8192
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula III:
                  wherein Ring D is a 5-7 membered monocyclic ring or 8-10
       membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or
       carbocyclyl; R.sup.x and R.sup.y are taken together with their
       intervening atoms to form a fused, unsaturated or partially unsaturated,
       5-8 membered carbocyclo ring; and R.sup.2 and R.sup.2' are as described
       in the specification. The compounds are useful as protein kinase
       inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating
       diseases such as cancer, diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo(4,3-c)pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo(4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPAT2
RN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

RN 404829-16-9 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-19-2 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN
     404829-23-8 USPAT2
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
CN
       5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA
       INDEX NAME)
```

```
L21 ANSWER 25 OF 40 USPAT2 on STN
ΑN
       2004:286776 USPAT2
       Fused pyrimidyl pyrazole compounds useful as protein kinase inhibitors
ΤI
       Bebbington, David, Newbury, UNITED KINGDOM
IN
       Binch, Hayley, Harwell, UNITED KINGDOM
       Knegtel, Ronald, Abingdon, UNITED KINGDOM
       Golec, Julian, Swindon, UNITED KINGDOM
       Patel, Sanjay, Abingdon, UNITED KINGDOM
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
       Kay, David, Purton, UNITED KINGDOM
       Davies, Robert, Arlington, MA, UNITED STATES
       Li, Pan, Arlington, MA, UNITED STATES
       Wannamaker, Marion, Stow, MA, UNITED STATES
       Forster, Cornelia, Pelham, NH, UNITED STATES
       Pierce, Albert, Somerville, MA, UNITED STATES
Vertex Pharmaceuticals, Incorporated, Cambridge, MA, UNITED STATES (U.S.
PA
       corporation)
       US----7008948
                            B2 20060307
       2003US-000624800
                                20030722 (10)
AΤ
       Division of Ser. No. 2001US-000952671, filed on 14 Sep 2001, Pat. No.
RLI
       US----6660731
PRAT
       2001US-000286949P
                            20010427 (60)
       2000US-000257887P
                            20001221 (60)
                                                                       <--
       2000US-000232795P
                            20000915 (60)
DT
       Utility
       GRANTED
FS
       Primary Examiner: McKenzie, Thomas C.
EXNAM
LREP
       Dixon, Lisa A.
CLMN
       Number of Claims: 16
       Exemplary Claim: 1
0 Drawing Figure(s); 0 Drawing Page(s)
ECL
DRWN
LN.CNT 8282
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula IV:
                   wherein Ring D is a 5-7 membered monocyclic ring or 8-10
       membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or
       carbocyclyl; R.sup.x and R.sup.y are independently selected from
       T-R.sup.3, or taken together with their intervening atoms to form a
       fused, unsaturated or partially unsaturated, 5-8 membered ring having
       1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen; and
       R.sup.2, R.sup.2', T, and R.sup.3 are as described in the specification.
       The compounds are useful as protein kinase inhibitors, especially as
       inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer,
       diabetes and Alzheimer's disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
       c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
       404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
       pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
       404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
```

c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN

CN

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPAT2
6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-18-1 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME) .

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-23-8 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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ANSWER 26 OF 40 USPAT2 on STN
L21
```

2004:216032 USPAT2 AN

Pyrazole compounds useful as protein kinase inhibitors ΤI

Bebbington, David, Newbury, UNITED KINGDOM IN

Charrier, Jean-Damien, Wantage, UNITED KINGDOM

Golec, Julian, Swindon, UNITED KINGDOM

Pierard, Fran.cedilla.oise, Drayton, UNITED KINGDOM

Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S. PA

corporation)

2004US-000775699

ΡI US----7427681 B2 20080923 20040210 (10)

Division of Ser. No. 2001US-000034019, filed on 20 Dec 2001, Pat. No. RLI

US----6727251 PRAI

20010427 (60) 2001US-000286949P 20001221 (60)

2000US-000257887P DT Utility

GRANTED

FS Primary Examiner: Wilson, James O.; Assistant Examiner: Truong, Tamthom **EXNAM**

LREP Chung, H. Joon

Number of Claims: 10 CLMN

ECI. Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2405

AΤ

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention describes novel pyrazole compounds of formula II: AB

> wherein Z.sup.1 is nitrogen or CR.sup.8; Q is --S--, --O--, --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.y, R.sup.2, and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-

```
c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPAT2
RN
CN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[(2-[2-(trifluoromethyl)phenyl]-4-quinazolinyl]amino]- (CA INDEX NAME)
```

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

404829-18-1 USPAT2 RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

ÇN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA TNDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 27 OF 40 USPAT2 on STN

AN 2004:172617 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Bebbington, David, Newbury, UNITED KINGDOM

Charrier, Jean-Damien, Wantage, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S.

corporation)

PI US----7087603 B2 20060808

AI 2003US-000736426 20031215 (10)

RLI Continuation of Ser. No. 2001US-000026966, filed on 19 Dec 2001,

ABANDONED

PRAI 2001US-000286949P 20010427 (60) . <-2000US-000257887P 20001221 (60) . <--

DT Utility

FS GRANTED

EXNAM Primary Examiner: Habte, Kahsay

LREP Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 8415

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula IV:

##STR1## wherein Z.sup.1 or Z.sup.2 is nitrogen, Q is --S--, --O--, --N(R.sup.4)--, --C(R.sup.6').sub.2--, 1,2-cyclopropanediyl, 1,2-cyclobutanediyl, or 1,3-cyclobutanediyl, and R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T--R.sup.3 or L--Z--R.sup.3, or R.sup.x and R.sup.y are taken together

with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPAT2 RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN

CN

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPAT2
6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-18-1 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

```
L21 ANSWER 28 OF 40 USPAT2 on STN
       2004:152232 USPAT2
AN
ΤI
       Pyrazole compounds useful as protein kinase inhibitors
       Davies, Robert, Arlington, MA, UNITED STATES
       Bebbington, David, Newbury, UNITED KINGDOM
       Knegtel, Ronald, Abingdom, UNITED KINGDOM
       Wannamaker, Marion, Stow, MA, UNITED STATES
       Li, Pan, Arlington, MA, UNITED STATES
       Forster, Cornelia, Pelham, NH, UNITED STATES
       Pierce, Albert, Somerville, MA, UNITED STATES
PΑ
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S.
       corporation)
       US----7390815
                           B2 20080624
PΤ
       2003US-000692355
                               20031023 (10)
       Division of Ser. No. 2001US-000955601, filed on 14 Sep 2001, Pat. No.
RLI
       US----6696452
PRAI
       2000US-000232795P
                           20000915 (60)
       2000US-000257887P
                           20001221 (60)
       2001US-000286949P
                           20010427 (60)
DΤ
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Habte, Kahsay
LREP
       Che, Jennifer G.
CLMN
       Number of Claims: 17
       Exemplary Claim: 1
ECL
DRWN
       No Drawings
LN.CNT 8330
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

This invention describes novel pyrazole compounds of formula II: ##STR1## wherein Ring C is selected from a phenyl, pyridinyl,

pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, and R.sup.2, R.sup.2', R.sup.x, and R.sup.y are as described in the specification. Ring C has an ortho substituent and is optionally substituted in the non-ortho positions. R.sup.2 and R.sup.2' are optionally taken together with their intervening atoms to form a fused ring system, such as an indazole ring; and R.sup.x and R.sup.y are optionally taken together with their intervening atoms to form a fused ring system, such as a quinazoline ring. The compounds are useful as protein kinase inhibitors, especially as inhibitors of GSK-3, for treating diseases such as diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine **404829-17-0P**, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
5-(2,4-dichlorophenyl)-1,5-dihydro-3-{(2-phenyl-4-quinazolinyl)amino}(CA INDEX NAME)

404829-22-7 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 29 OF 40 USPAT2 on STN

2004:127517 USPAT2 ΑN

Triazole compounds useful as protein kinase inhibitors ΤI

Bebbington, David, Newbury, UNITED KINGDOM Knegtel, Ronald, Abingdom, UNITED KINGDOM Binch, Hayley, Harwell, UNITED KINGDOM IN

Golec, Julian M. C., Faringdon, UNITED KINGDOM Li, Pan, Arlington, MA, UNITED STATES

Charier, Jean-Damien, Wantage, UNITED KINGDOM

Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S. PΑ

corporation)
US----7115739 B2 20061003 ΡI

ΑI 2001US-000953471 20010914 (9)

PRAI 2001US-000286949P 20010427 (60)

20001221 (60) 2000US-000257887P 20000915 (60) 2000US-000232795P

DT Utility

GRANTED FS

EXNAM Primary Examiner: McKenzie, Thomas C.

LREP Dixon, Lisa A., Che, Jennifer G., Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 8169

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel triazole compounds of formula IX:

##STR1## wherein Z.sup.1 is nitrogen or CR.sup.9 and Z.sup.2 is nitrogen or CH, provided that at least one of Z.sup.1 and Z.sup.2 is nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T-R.sup.3, or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused ring; R.sup.1; R.sup.3, and T are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of GSK-3 and Aurora, for treating diseases such as diabetes, cancer, and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino] - (CA INDEX NAME)

404829-17-0 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

. 5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-21-6 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl}- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 30 OF 40 USPAT2 on STN

AN 2003:120843 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Davies, Robert, Arlington, MA, United States
Li, Pan, Arlington, MA, United States
Golec, Julian M. C., Swindon, UNITED KINGDOM
Charrier, Jean-Damien, Wantage, UNITED KINGDOM
Knegtel, Ronald, Abingdom Oxon, UNITED KINGDOM

Bebbington, David, Newbury, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S. corporation)

```
РΤ
       US----6610677
                           B2 20030826
       2001US-000952833
                               20010914 (9)
ΑI
PRAI
                           20010427 (60)
       2001US-000286949P
       2000US-000257887P
                           20001221 (60)
                           20000915 (60)
       2000US-000232795P
DT
       Utility
FS
       GRANTED
       Primary Examiner: Raymond, Richard L.; Assistant Examiner: McKenzie,
EXNAM
LREP
       Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated
CLMN
       Number of Claims: 16
ECL
       Exemplary Claim: 1
DRWN
       0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 8363
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compositions comprising a
       pharmaceutically acceptable carrier and a compound of formula VIII:
       ##STR1##
```

wherein Z.sup.1 is N or C--R.sup.9, Z.sup.2 is N or CH, and Z.sup.3 is N or C--R.sup.x, provided that one of Z.sup.1 and Z.sup.3 is nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.x, R.sup.1, R.sup.2, R.sup.2', R.sup.3, and R.sup.9 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
     pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPAT2
RN
CN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA TNDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

RN

CN

404829-21-6 USPAT2
6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-22-7 USPAT2 RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
L21 ANSWER 31 OF 40 USPAT2 on STN
       2003:113534 USPAT2
       Pyrazole compounds useful as protein kinase inhibitors
TΙ
       Bebbington, David, Newbury, UNITED KINGDOM
ΤN
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
Davies, Robert, Arlington, MA, United States
       Golec, Julian M. C., Swindon, UNITED KINGDOM
Kay, David, Purton, UNITED KINGDOM
       Knegtel, Ronald, Abingdon, UNITED KINGDOM
       Patel, Sanjay, Abingdon, UNITED KINGDOM
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.
PA
       corporation)
PΤ
       US----6653301
                            B2 20031125
                                 20011219 (10)
       2001US-000027001
AΤ
                            20010427 (60)
       2001US-000286949P
PRAI
       2000US-000257887P
                            20001221 (60)
       Utility
DT
FS
       GRANTED
       Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker
EXNAM
       Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated
LREP
       Number of Claims: 26
.CLMN
       Exemplary Claim: 1
ECL
       O Drawing Figure(s); O Drawing Page(s)
DRWN
LN.CNT 8765
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
        This invention describes novel pyrazole compounds of formula IIa:
AΒ
        wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic
        ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl,
        heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are taken together with
       their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and
        R.sup.2 are as described in the specification. The compounds are useful
        as protein kinase inhibitors, especially as inhibitors of Aurora-2 and
        GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's
        disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
       c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
       404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
       pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
       404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
       c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
       [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
       yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
       [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
       yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
       [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
       c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
       [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
       yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
       [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
       phenylquinazolin-4-yl)amine
         (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
         analogs as protein kinase inhibitors for treatment of cancer, diabetes,
         and Alzheimer's disease)
      404827-31-2 USPAT2
 RN
      6H-Pyrazolo[4,3-c]pyridazin-6-one,
 CN
        1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
        guinazolinyl]amino]- (CA INDEX NAME)
```

404829-16-9 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-18-1 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 32 OF 40 USPAT2 on STN

2003:113425 USPAT2 AN

TT Pyrazole compounds useful as protein kinase inhibitors

IN Davies, Robert, Arlington, MA, United States Bebbington, David, Newbury, UNITED KINGDOM Knegtel, Ronald, Abingdom, UNITED KINGDOM Wannamaker, Marion, Stow, MA, United States Li, Pan, Arlington, MA, United States

Forster, Cornelia, Pelham, NH, United States

Pierce, Albert, Somerville, MA, United States

Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S. PA

corporation)

US----6696452 B2 20040224

2001US-000955601 20010914 (9) ΑI PRAI 2000US-000232795P 20000915 (60)

2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60)

DT Utility

ΡI

GRANTED FS

EXNAM Primary Examiner: Berch, Mark L.; Assistant Examiner: Habte, Kahsay

Robidoux, Andrea L.C., Vertex Pharmaceuticals Incorporated Number of Claims: 21 T.REP

CLMN

Exemplary Claim: 1

DRWN O Drawing Figure(s); O Drawing Page(s)

LN.CNT 8476

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention describes novel pyrazole compounds of formula II: ##STR1##

> wherein Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, and R.sup.2, R.sup.2', R.sup.x, and R.sup.y are as described in the specification. Ring C has an ortho substituent and is optionally substituted in the non-ortho positions. R.sup.2 and R.sup.2' are optionally taken together with their intervening atoms to form a fused ring system, such as an indazole ring; and R.sup.x and R.sup.y are optionally taken together with their intervening atoms to form a fused ring system, such as a quinazoline ring. The compounds are useful as protein kinase inhibitors, especially as inhibitors of GSK-3, for treating diseases such as diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-

yl] (2-phenylquinazolin-4-yl) amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl] (2-phenylquinazolin-4-yl) amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-16-9 USPAT2
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 404829-17-0 USPAT2
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-18-1 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl] - (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

CN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-23-8 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

```
ANSWER 33 OF 40 USPAT2 on STN
L21
       2003:106775 USPAT2
ΑN
       Pyrazole compounds useful as protein kinase inhibitors
ΤI
       Bebbington, David, Newbury Berkshire, UNITED KINGDOM
IN
       Binch, Hayley, Harwell, UNITED KINGDOM
       Knegtel, Ronald, Abingdom, UNITED KINGDOM
       Golec, Julian, Swinden, UNITED KINGDOM
       Patel, Sanjay, Abingdom, UNITED KINGDOM
Charrier, Jean- Damien, Southam, UNITED KINGDOM
       Kay, David, 4 Church Path, UNITED KINGDOM
       Davies, Robert, Arlington, MA, United States
       Li, Pan, Arlington, MA, United States
       Wannamaker, Marion, Stow, MA, United States
       Forster, Cornelia, Pelham, NH, United States
       Pierce, Albert, Somerville, MA, United States
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.
PΑ
       corporation)
       115----6660731
                                20031209
PΙ
                                                                        <--
       2001US-000952671
                                 20010914 (9)
ΑI
                                                                        <--
       2001US-000286949P
                            20010427 (60)
PRAI
                                                                        <--
       2000US-000257887P
                            20001221 (60)
                            20000915 (60)
       2000US-000232795P
DT
       Utility
       GRANTED
FS
       Primary Examiner: Raymond, Richard L.; Assistant Examiner: McKenzie,
EXNAM
       Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated
LREP
       Number of Claims: 15
CĹMN
ECL
       Exemplary Claim: 1
DRWN
       O Drawing Figure(s); O Drawing Page(s)
LN.CNT 8222
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
        This invention describes novel pyrazole compounds of formula IV:
        ##STR1##
```

wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from

T-R.sup.3, or taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-8 membered ring having 1-3 ring heteroatoms selected from oxygen, sulfur, or nitrogen; and R.sup.2, R.sup.2, T, and R.sup.3 are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine $(protein\ kinase\ inhibitor;\ preparation\ of\ heterocyclylpyrazolamines\ and$ analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPAT2 RN CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, $1, 5- dihydro-5- phenyl-3- \hbox{\tt [[2-[2-(trifluoromethyl)phenyl]-4-}\\$ quinazolinyl]amino] - (CA INDEX NAME)

INDEX NAME)

RN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

RN

CN

404829-18-1 USPAT2
6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one; CN

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

404829-22-7 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]-INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-23-8 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 34 OF 40 USPAT2 on STN

2003:93620 USPAT2

Pyrazole compounds useful as protein kinase inhibitors ΤI

ΤN

Knegtel, Ronald, Abingdom, UNITED KINGDOM Bebbington, David, Newbury Berkshire, UNITED KINGDOM

Binch, Hayley, Harwell, UNITED KINGDOM Golec, Julian, Swinden, UNITED KINGDOM Patel, Sanjay, Abingdom, UNITED KINGDOM

Charrier, Jean-Damien, Bishop's Itchington, UNITED KINGDOM

Kay, David, Purton Wiltshire, UNITED KINGDOM

Davies, Robert, Arlington, MA, United States

Li, Pan, Arlington, MA, United States

Wannamaker, Marion, Stow, MA, United States Forster, Cornelia, Pelham, NH, United States

Pierce, Albert, Somerville, MA, United States

Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.

corporation)

PΑ

PΙ

US----6613776 B2 20030902 ΑI 2001US-000952836 20010914 (9) 2000US-000232795P 20000915 (60) PRAT 2000US-000257887P 20001221 (60) 2001US-000286949P 20010427 (60) DTUtility FS GRANTED EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Balasubramanian, Venkataraman LREP Shair, Karoline K.M., Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated CLMN Number of Claims: 28 ECL Exemplary Claim: 1 DRWN 0 Drawing Figure(s); 0 Drawing Page(s) LN.CNT 8825 CAS INDEXING IS AVAILABLE FOR THIS PATENT. This invention describes novel pyrazole compositions comprising a pharmaceutically acceptable carrier and a compound of formula V: ##STR1##

wherein Z.sup.1 is N, CR.sup.a, or CH, and Z.sup.2 is N or CH, provided one of Z.sup.1 and Z.sup.2 is nitrogen; G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T--R.sup.3, or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused ring; and R.sup.1, R.sup.2, R.sup.2', R.sup.3, and T are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN 404829-16-9 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-21-6 USPAT2

RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-23-8 USPAT2

RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

```
L21 ANSWER 35 OF 40 USPAT2 on STN
       2003:79141 USPAT2
AN
       Pyrazole compounds useful as protein kinase inhibitors
TI
IN
       Bebbington, David, Newbury, UNITED KINGDOM
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
       Davies, Robert, Arlington, MA, UNITED STATES
       Everitt, Simon, Beaconsfield, UNITED KINGDOM
       Kay, David, Purton, UNITED KINGDOM
       Knegtel, Ronald, Abingdon, UNITED KINGDOM
       Patel, Sanjay, Abingdon, UNITED KINGDOM
PΑ
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, UNITED STATES (U.S.
       corporation)
       US----6989385
PΤ
                           B2 20060124
       2001US-000026967
                               20011219 (10)
                                                                     <--
ΑI
                                                                     <--
       2000US-000257887P
                           20001221 (60)
PRAI
       2001US-000286949P
                           20010427 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Rao, Deepak
LREP
       Dixon, Lisa A.
       Number of Claims: 31
CLMN
       Exemplary Claim: 1
ECL
       O Drawing Figure(s); O Drawing Page(s)
DRWN
LN.CNT 8598
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention describes novel pyrazole compounds of formula IIc:
       ##STR1##
       wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic
       ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl,
       heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are taken together with
       their intervening atoms to form a fused, unsaturated or partially
       unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and
       R.sup.2' are as described in the specification. The compounds are useful
       as protein kinase inhibitors, especially as inhibitors of Aurora-2 and
       GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's
       disease.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo(4,3-
      c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
      404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-
      pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo(4,3-
      c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPAT2
RN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
CN
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

RN 404829-16-9 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-17-0 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 - ANSWER 36 OF 40 USPAT2 on STN

AN 2003:79117 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Davies, Robert J., Arlington, MA, United States
Li, Pan, Arlington, MA, United States
Charrier, Jean-Damien, Wantage, UNITED KINGDOM
Bebbington, David, Newbury, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.

corporation)

PI US----6638926 B2 20031028

AI 2001US-000953505 20010914 (9) <--

PRAI 2000US-000232795P 20000915 (60) <-2000US-000257887P 20001221 (60) <--

2001US-000286949P 20010427 (60) <--

DT Utility

FS GRANTED

EXNAM Primary Examiner: Berch, Mark L.; Assistant Examiner: Habte, Kahsay

LREP Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 27

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 8654

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides novel pyrazole compounds that are useful as protein kinase inhibitors, especially as inhibitors of aurora-2 and GSK-3. The compounds may be used to treat abnormal physiological function leading to diseases such as cancer, diabetes and Alzheimer's disease. The compounds are represented by formula VI: ##STR1##

wherein G is Ring C or Ring D; Ring C is selected from a phenyl, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl ring, wherein said Ring C has one or two ortho substituents independently selected from --R.sup.1; Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.y is T--R.sup.3'; T is a valence bond or a C.sub.1-4 alkylidene chain; R.sup.3' is an optionally substituted group selected from C.sub.1-6 aliphatic, C.sub.3-10 carbocyclyl, C.sub.6-10 aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms; and R.sup.1, R.sup.2, and R.sup.2' are as described in the specification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine
404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
[5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 40429-19-2P,
[5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-

yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN $1,5-{\tt dihydro-5-phenyl-3-[\{2-[2-(trifluoromethyl)phenyl]-4-[}]$ quinazolinyl]amino] - (CA INDEX NAME)

RN

CN

RN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 404829-18-1 USPAT2
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

 $\label{localization} 1,5-{\tt dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino]-} \quad ({\tt CA})$ INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-22-7 USPAT2

RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

```
L21 ANSWER 37 OF 40 USPAT2 on STN
```

AN 2003:51585 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Bebbington, David, Newbury, UNITED KINGDOM
Charrier, Jean-Damien, Wantage, UNITED KINGDOM
Golec, Julian, Swindon, UNITED KINGDOM
Miller, Andrew, Didcot, UNITED KINGDOM

Knegtel, Ronald, Abingdon, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.

corporation)

PI US----6664247 B2 20031216

AI 2001US-000025164 20011219 (10) <--

PRAI 2000US-000257887P 20001221 (60) <-2001US-000286949P 20010427 (60) <--

DT Utility

FS GRANTED

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker B.

LREP Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 8702

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula IIIa: ##STR1##

wherein R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x, R.sup.y, R.sup.2, and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-

```
pyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine
      404829-17-0P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3-
      c)pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P,
      [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-19-2P,
      [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-21-6P,
      [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo(4,3-
      c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P,
      [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-
      yl](2-phenylquinazolin-4-yl)amine 404829-23-8P,
      [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2-
      phenylquinazolin-4-yl)amine
        (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and
        analogs as protein kinase inhibitors for treatment of cancer, diabetes,
        and Alzheimer's disease)
     404827-31-2 USPAT2
RN
CN
     6H-Pyrazolo[4,3-c]pyridazin-6-one,
       1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4-
       quinazolinyl]amino]- (CA INDEX NAME)
```

404829-18-1 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]-INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

5-(2,4-dichlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

CN

6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 38 OF 40 USPAT2 on STN

AN 2003:30936 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Bebbington, David, Newbury, UNITED KINGDOM Charrier, Jean-Damien, Wantage, UNITED KINGDOM

Golec, Julian, Swindon, UNITED KINGDOM Pierard, Francoise, Drayton, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.

corporation)
PI US----67272

US----6727251 B2 20040427

AI 2001US-000034019 20011220 (10)

PRAI 2000US-000257887P 20001221 (60) <-2001US-000286949P 20010427 (60) <--

DT Utility

FS GRANTED

EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Truong, Tamthom N.

LREP Robidoux, Andrea L. C., Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 2107

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula II: ##STR1##

wherein Z.sup.1 is nitrogen or CR.sup.8; Q is --S--, --O--, --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.y, R.sup.2, and R.sup.2' are as described in the specification.

The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-0xo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine **404829-16-9P**, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPAT2
CN 6H-Pyrazolo(4,3-c)pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

404829-18-1 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino)- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA TNDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

L21 ANSWER 39 OF 40 USPAT2 on STN

AN 2003:4125 USPAT2

TI Pyrazole compounds useful as protein kinase inhibitors

IN Bebbington, David, Newbury, UNITED KINGDOM Charrier, Jean-Damien, Wantage, UNITED KINGDOM

PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.

corporation)

PI US----6656939 B2 20031202

AI 2001US-000034683 20011220 (10)
PRAT 2000US-000257887P 20001221 (60)

I 2000US-000257887P 20001221 (60) <--

2001US-000286949P 20010427 (60) DT Utility

FS GRANTED

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Balasubramanian, Vankataraman

LREP Shair, Karoline K.M., Vertex Pharmaceuticals Incorporated

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN 0 Drawing Figure(s); 0 Drawing Page(s)

LN.CNT 2110

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention describes novel pyrazole compounds of formula III: ##STR1##

wherein Z.sup.1, Z.sup.2, and Z.sup.3 are as described in the specification; Q is --S--, --O--, --N(R.sup.4)--, or --CH(R.sup.6)--; R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases

<--.

such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-Oxo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-Oxo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine $(protein\ kinase\ inhibitor;\ preparation\ of\ heterocyclylpyrazolamines\ and$ analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) RN 404827-31-2 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[[2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

RN

CN

RN

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-16-9 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-17-0 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

RN

404829-18-1 USPAT2 6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-5-(4-methoxyphenyl)-3-((2-phenyl-4-quinazolinyl)amino)- (CA

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-19-2 USPAT2 RN

6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

404829-21-6 USPAT2 RN

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 404829-22-7 USPAT2

RN 404829-22-7 USPAT2 CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX'NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

##STR1##

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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L21 ANSWER 40 OF 40 USPAT2 on STN AN 2003:4122 USPAT2
       Pyrazole compounds useful as protein kinase inhibitors
       Bebbington, David, Newbury, UNITED KINGDOM
IN
       Charrier, Jean-Damien, Wantage, UNITED KINGDOM
       Golec, Julian, Swindon, UNITED KINGDOM
       Green, Jeremy, Burlington, MA, United States
       Kay, David, Purton, UNITED KINGDOM
       Knegtel, Ronald, Abingdon, UNITED KINGDOM
Miller, Andrew, Didcot, UNITED KINGDOM
       Tomlison, Ronald, Marlborough, MA, United States
       Li, Pan, Arlington, MA, United States
       Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S.
PA
       corporation)
                             B2 20031125
       US----6653300
PΤ
       2001US-000026975
                                 20011219 (10)
AΙ
                             20010427 (60)
                                                                         <--
PRAI
       2001US-000286949P
       2000US-000257887P
                             20001221 (60)
DΤ
       Utility
       GRANTED
EXNAM
       Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker
       Robidout, Andrea L. C., Vertex Pharmaceuticals Incorporated
LREP
CLMN
       Number of Claims: 40
        Exemplary Claim: 1
ECL
        O Drawing Figure(s); O Drawing Page(s)
DRWN
LN.CNT 8954
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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This invention describes novel pyrazole compounds of formula I':

wherein Q' is --O--, --C(R.sup.6').sub.2--, 1,2-cyclopropanediyl, 1,2-cyclobutanediyl, or 1,3-cyclopropanediyl, and R.sup.1 is T-Ring D, wherein Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl; R.sup.x and R.sup.y are independently selected from T--R.sup.3 or L--Z--R.sup.3, or R.sup.x and R.sup.y are taken together with their intervening atoms to form a fused, unsaturated or partially unsaturated, 5-7 membered ring having 0-3 heteroatoms; and R.sup.2 and R.sup.2' are as described in the specification. The compounds are useful as protein kinase inhibitors, especially as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes and Alzheimer's disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT. IT 404827-31-2P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-[2-(2-trifluoromethylphenyl)quinazolin-4-yl]amine 404829-16-9P, [5-(3-Methoxyphenyl)-6-oxo-5,6-dihydro-1Hpyrazolo[4,3-c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-17-0P, (6-Oxo-5-phenyl-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl)-(2-phenylquinazolin-4-yl)amine 404829-18-1P, [5-(4-Methoxyphenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-19-2P, [5-(2,4-Dichlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-21-6P, [6-0xo-5-(3-trifluoromethylphenyl)-5,6-dihydro-1H-pyrazolo[4,3c]pyridazin-3-yl](2-phenylquinazolin-4-yl)amine 404829-22-7P, [6-0xo-5-(4-Phenoxyphenyl)-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3yl](2-phenylquinazolin-4-yl)amine 404829-23-8P, [5-(4-Chlorophenyl)-6-oxo-5,6-dihydro-1H-pyrazolo[4,3-c]pyridazin-3-yl](2phenylquinazolin-4-yl)amine (protein kinase inhibitor; preparation of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease) 404827-31-2 USPAT2 RN 6H-Pyrazolo[4,3-c]pyridazin-6-one, 1,5-dihydro-5-phenyl-3-([2-[2-(trifluoromethyl)phenyl]-4quinazolinyl]amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-16-9 USPAT2
CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,
1,5-dihydro-5-(3-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA
TNDEX NAME)

RN 404829-17-0 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-phenyl-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-18-1 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-methoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE .

RN 404829-19-2 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(2,4-dichlorophenyl)-1,5-dihydro-3-((2-phenyl-4-quinazolinyl)amino)-(CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-21-6 USPAT2

6H-Pyrazolo[4,3-c]pyridazin-6-one, CN

1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

RN 404829-22-7 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

1,5-dihydro-5-(4-phenoxyphenyl)-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 404829-23-8 USPAT2

CN 6H-Pyrazolo[4,3-c]pyridazin-6-one,

5-(4-chlorophenyl)-1,5-dihydro-3-[(2-phenyl-4-quinazolinyl)amino]- (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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FILE 'REGISTRY' ENTERED AT 10:33:15 ON 05 DEC 2008

FILE 'HCAPLUS' ENTERED AT 10:33:18 ON 05 DEC 2008 1 US20040192682 /PN

FILE 'REGISTRY' ENTERED AT 10:33:36 ON 05 DEC 2008

FILE 'HCAPLUS' ENTERED AT 10:33:36 ON 05 DEC 2008 L2 TRA L1 1- RN : 44 TERMS

FILE 'REGISTRY' ENTERED AT 10:33:37 ON 05 DEC 2008

L3 44 SEA L2

L4 36 L3 AND N2C3-N2C4/ES

L5 STR

L6 STR L5

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L7
             4 L6
L8
             82 L6 FULL
             36 L8 AND L3
L9
L10
                STR L5
L11
                STR L6
L12
              2 (L10 OR L11) SUB=L8 SAM
             41 (L10 OR L11) FULL SUB=L8
L13
L14
             27 L13 AND L3
             14 L13 NOT L14
L15
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L16
             1 L14
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L21
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L22
              0 L14
              0 L15
L23
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AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Previously presented) A compound of formula I:

I

or a pharmaceutically acceptable salt or mixtures thereof,

wherein R¹ is selected from -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; L is an optionally substituted C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O); m is 0 or 1; Ar¹ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and Cy¹ is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Ar¹ and Cy¹ are each independently optionally substituted with y occurrences of Z-R^Y; wherein Z is a bond or is a C₁-C₆ alkylidene chain wherein up to two non-adjacent methylene units of Z are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO₂, NRCONR, NRCSNR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; each occurrence of R^Y is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', CO_2R' , OC(O)R', $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, SOR', SO_2R' , $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, C(O)C(O)R', or $C(O)CH_2C(O)R'$; and y is 0-5;

R² is selected from halogen, NO₂, -SR, -N(R)₂, -(T)_nR, or -(T)_nAr² wherein T is an optionally substituted C₁₋₄ alkylidene chain wherein up to two non-adjacent methylene units of T are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO2, CO, CO2, CONR, CSNR, OC(O)NR, SO2, SO2NR, NRSO2, NRSO2NR, C(O)C(O), or $C(O)CH_2C(O)$; n is 0 or 1; Ar^2 is an optionally substituted aryl group selected from a 5-6 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur wherein Ar² is independently optionally substituted with up to five substituents selected from Q-R^X; wherein Q is a bond or is a C₁-C₆ alkylidene chain wherein up to two non-adjacent methylene units of Q are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO2, NRCONR, NRCSNR, SO, SO2. NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^X is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', $NR'C(O)N(R')_2$, $NR'C(S)N(R')_2$, $NR'CO_2R'$, C(O)R', CO_2R' , OC(O)R', $C(O)N(R')_2$, $C(S)N(R')_2$, $OC(O)N(R')_2$, SOR', SO_2R' , $SO_2N(R')_2$, $NR'SO_2R'$, $NR'SO_2N(R')_2$, C(O)C(O)R', or C(O)CH₂C(O)R';

 R^3 is hydrogen or an optionally substituted C_{1-4} aliphatic group; X is selected from a valence bond, O, S, or NR:

R⁴ is selected from -R, -U-Ar³, or -(U)_jCy³; U is an optionally substituted C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of U are optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NRCO₂, CO, CO₂, CONR, CSNR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O); j is 0 or 1; Ar³ is an optionally substituted aryl group selected from a 3-8 membered monocyclic or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and Cy³ is an optionally substituted group selected from a 3-7-membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10-membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein Ar³ and Cy³ are each independently optionally substituted with up to five substituents selected from Y-R^Z; wherein Y is a bond or is a C₁-C₆ alkylidene chain wherein up to two non-adjacent

methylene units of Y are optionally replaced by CO, CO₂, COCO, CONR, CSNR, OCONR, NRNR, NRNRCO, NRCO, NRCS, NRCO₂, NRCONR, NRCSNR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; and each occurrence of R^Z is independently selected from R', halogen, NO₂, CN, OR', SR', N(R')₂, NR'C(O)R', NR'C(S)R', NR'C(O)N(R')₂, NR'C(S)N(R')₂, NR'CO₂R', C(O)R', CO₂R', OC(O)R', C(O)N(R')₂, C(S)N(R')₂, OC(O)N(R')₂, SOR', SO₂R', SO₂N(R')₂, NR'SO₂R', NR'SO₂N(R')₂, C(O)C(O)R', or C(O)CH₂C(O)R'; or

wherein R⁴ and R, taken together with the nitrogen form an optionally substituted 5-8 membered heterocyclyl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each occurrence of R is independently selected from hydrogen or an optionally substituted C₁₋₆ aliphatic group, or two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and

each occurrence of R' is independently selected from hydrogen or an optionally substituted group selected from C_{1-6} aliphatic, C_{6-10} aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 3-10 ring atoms, or wherein two R on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur,

provided that:

- a) when X is NR; R, R³, and R⁴ are each hydrogen; R² is $-(T)_n R$ wherein n is 0 and R is hydrogen; and R¹ is $-(L)_m A r^1$ wherein m is 0; then $A r^1$ is not:
 - i) 4-Cl or 4-OMe phenyl; or
 - ii) 3-CF₃ phenyl;
- d) when X is a valence bond; R^4 is hydrogen; R^3 is CH_3 ; R^2 is either chloro or hydrogen; and R^1 is $-(L)_mAr^1$ wherein m is 0, then Ar^1 is not 3-trifluoromethyl phenyl or 2-fluoro-5-trifluoromethyl phenyl;
- f) when X is a valence bond; R^4 is methyl; R^2 is $-(T)_nR$ wherein n is 0 and R is hydrogen; R^3 is hydrogen; and R^1 is $-(L)_mAr^1$ wherein m is 0; then Ar^1 is not 4-tolyl;